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10/758,902	01/16/2004	Fiorenzo Stirpe	PNJ-005CN	7360

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,902	STIRPE ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☒ Claim(s) *11-14 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/445,160.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending.

Election/Restrictions

This Election/Restriction requirement replaces the Election/Restriction requirement mailed December 1, 2005.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to a ribosome-inactivating polypeptide, classified in class 435, subclass 199.

II. Claims 11-20, drawn to a polynucleotide encoding a ribosome-inactivating polypeptide, vector, host cell, and recombinant method of making the encoded protein, classified in class 536, subclass 23.2.

Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Also, product and process inventions are distinct if any of the following can be shown: (1) that the process as claimed can be used to make another and materially different product, (2) that the product claimed can be used in a materially different process of using that product, or (3) that the product claimed can be made by another and materially different process (MPEP § 806.05(h)). These inventions are different or distinct for the following reasons.

The polynucleotide of Invention II is related to the polypeptide of Invention I by virtue of encoding the same. The DNA molecule has utility for the recombinant production of the polypeptide in host cells. Although the DNA molecule and polypeptide are related, since the

DNA encodes the specifically claimed polypeptide, they are distinct inventions because they are physically and functionally distinct chemical entities, and the polypeptide product can be made by another and materially different process, such as by synthetic peptide synthesis or purification from the natural source. Further, the DNA may be used for processes other than the production of the polypeptide, such as in a nucleic acid hybridization assay.

The search of Invention II would not encompass a search for Invention I, which would include searching the prior art for teachings of the purified polypeptide. Conversely, a search for Invention I, class 435, subclass 199, would not encompass a search for Invention II, which would include searching class 536, subclass 23.2. Thus, a search of either Invention I or II would not encompass a search for the other invention and searching both inventions would be a burden on the Office.

These inventions are distinct for the reasons given above and have acquired a separate status in the art due to their recognized divergent subject matter, as shown by their different classification. Furthermore, as explained above, searching more than one invention would be a burden on the Office. Therefore, restriction for examination purposes, as indicated, is proper.

During a telephone conversation with Jane Remillard on April 3, 2005 a provisional election was made without traverse to prosecute the invention of II, Claims 11-20. Affirmation of this election must be made by Applicant in replying to this Office action. Claims 1-10 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 11-20 are herein examined.

Priority

The priority date of the instant invention is taken to be June 6, 1997, the filing date of EPO 97201725.5.

Drawings-Objections

Figure 3 is objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to correct Figure 3, or the legend thereto, to identify all of the sequences disclosed therein by sequence identifier numbers.

Abstract-Objection

The Abstract is objected to because the first phrase is a run-on sentence.

Specification-Objections

The specification should be up-dated to reflect the issuance of US 09/445,160.

The specification is objected to because the results presented in Table 2 have no units.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object e.g., "We claim" or "The claims are".

Claims 11, 12, 14, and 17 are objected to for improper antecedent usage as follows.

For Claim 11, "a protein according to claim 1" should be "the protein according to claim 1".

For Claim 12, "an oligonucleotides or polynucleotide sequence according to claim 10" should be "the oligonucleotides or polynucleotide sequence according to claim 10".

For Claim 14, "a recombinant vector of claim 12" should be "the recombinant vector of claim 12".

For Claim 17, the phrase "the expressed recombinant bouganin" on line 7, should be "the expressed recombinant bouganin-ligand fusion protein".

Claims 11-14 are objected to for being dependent from non-elected claims.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Claims 12-14 are indefinite because they are improperly dependent. Claim 12 recites "oligonucleotides or polynucleotide sequence according to claim 10" but Claim 10 recites a pharmaceutical composition comprising a polypeptide, not a nucleic acid sequence. Claims 13

and 14, as dependent from Claim 12, are indefinite for the same reason. For purposes of examination, it is assumed that Claim 12 is meant to be dependent from Claim 11.

For Claim 11, the phrase "comprising a sequence of at least 15, especially at least 24 nucleotides" is indefinite for the two reasons. (1) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). In the present instance, Claim 11 recites the broad recitation of at least 15 nucleotides, and the claim also recites at least 24 nucleotides, which is the narrower statement of the range/limitation. (2) It is unclear whether the phrase "comprising a sequence of at least 15, especially at least 24 nucleotide" modifies "oligonucleotides or polynucleotide" or "part thereof". Claims 12-14, as dependent from Claim 11, are rejected under 35 U.S.C. 112, second paragraph, for the same reasons.

For Claim 11, it is unclear whether the phrase "or part thereof" modifies "oligonucleotides or polynucleotide" or "protein according to claim 1". Claims 12-14, as dependent from Claim 11, are rejected under 35 U.S.C. 112, second paragraph, for the same reasons.

For Claim 11, the term "equivalent" in Claim 1 renders the dependent claim, Claim 11, indefinite. "Equivalent" is not defined by the claim or the specification and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Clarification is required. Claims 12-14, as dependent from Claim 11, are rejected under 35 U.S.C. 112, second paragraph, for the same reasons.

For Claim 13, it is unclear whether the phrase "oligonucleotide sequence" on line 3 is meant to be "oligonucleotide or polynucleotide sequence". Clarification is required.

For Claims 15 and 17, it is unclear whether the term "bouganin" refers to the specific protein purified in Example 1, or a genus of proteins having the following characteristics, as recited in the specification (page 1, lines 3-9).

> "The invention discloses a new type-1 ribosome-inactivating protein (RIP), referred to as bouganin, isolated from the leaves of Bougainvillea species, especially B. spectabilis Willd. Bouganin differs from other type-1 RIP by its unique amino acid composition. Bouganin has a molecular weight of about 26,200 daltons."

Clarification is required. Claim 16 and Claims 18-20, as dependent from Claims 15 and 17, respectively, are indefinite for the same reason. For purposes of examination, it is assumed that "bouganin" refers the genus of proteins having the above characteristics.

For Claim 19, the terms "large" and "small" are relative terms, which renders the claim indefinite. The terms "large" and "small" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Clarification is required. Claim 20, as dependent from Claim 19, is indefinite for the same reason.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 11-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for any polynucleotide encoding any RIP of ~26kD, pI

9.0, and having at the N-terminus, a sequence having at least 50% homology to SEQ ID NO: 1 or any recombinant method of making any bouganin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 11-14 are so broad as to encompass any polynucleotide encoding any RIP of ~26kD, pI 9.0, and, at the N-terminus, a sequence having at least 50% homology to SEQ ID NO: 1 as well as vectors and host cells comprising said RIP-encoding polynucleotides. Claims 15-20 are so broad as to encompass recombinant methods of making any bouganin, wherein a bouganin is defined as a RIP isolated from any Bougainvillea species and having a molecular weight of ~26kD. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional

properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired RIP activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 11-14 which, encompasses all peptides having RIP activity and having a molecule weight of ~26kD, a pI of 9.0, and an N-terminal a sequence having at least 50% homology to SEQ ID NO: 1 as well as vectors and host cells comprising said RIP-encoding polynucleotides. The specification also does not support the broad scope of Claim 15-20, which encompasses recombinant methods of making all RIPs isolated from any Bougainvillea species and having a molecular weight of ~26kD. The specification does not support the broad scope of Claims 11-20 because the specification does not establish: (A) the structure of any polynucleotide encoding any RIP from any Bougainvillea species; (B) the structure of all RIPs of ~26kD, a pI of 9.0, and an N-terminal a sequence having

at least 50% homology to SEQ ID NO: 1 or the encoding polynucleotides; (C) the structure of all RIPs isolated from Bougainvillea species and having a molecular weight of ~26kD or the encoding polynucleotides; (D) regions of the proteins' structure which may be modified without effecting the RIP activity; (E) the general tolerance of the RIP activity to modification and extent of such tolerance; (F) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (G) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide encoding any number of RIPs with an enormous number of amino acid modifications of the RIP of Example 1 or encoding any RIP from any Bougainvillea species. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 11-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 11-14 are directed to a genus of nucleic acid molecules encoding RIP molecules having a molecule weight of ~26kD, a pI of 9.0, and an N-terminal a sequence having at least 50% homology to SEQ ID NO: 1 as well vectors and host cells comprising said RIP-encoding polynucleotides. Claims 15-20 are directed to a genus of recombinant methods for making any RIP molecule isolated from Bougainvillea species and having a molecular weight of ~26kD. The specification teaches no such nucleic acid molecules or recombinant method methods of making the encoded proteins. Moreover, the specification fails to describe any representative species of said nucleic acid molecules by any identifying characteristics or properties other than the functionality of encoding a RIP having a molecule weight of ~26kD, a pI of 9.0, and an N-terminal a sequence having at least 50% homology to SEQ ID NO: 1 or a RIP of ~26kD from any Bougainvillea species. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that Applicants identify support, within the original application, for any amendments to the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1656